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Sylvie Sauvaigo

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WILLIAM E. BEAUMONT
1901 L. STREET NW, SUITE 800
WASHINGTON, DC 20036

EXAMINER

JOIKE, MICHELE K

ART UNIT

PAPER NUMBER

1636

MAIL DATE

DELIVERY MODE

09/04/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/539,769	Applicant(s) SAUVAIGO, SYLVIE	
	Examiner MICHELE K. JOIKE	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 April 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 22-50 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 22-50 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Receipt is acknowledged of a reply to the previous Office Action, filed April 29, 2008.

Claims 22-50 are pending, with and examined. Any rejection of record in the previous Office Action, mailed December 14, 2007 that is not addressed in this action has been withdrawn.

Because this Office Action only maintains rejections set forth in the previous Office Action and/or sets forth new rejections that are necessitated by amendment, this Office Action is made FINAL.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 22-25, 31, 33, 38, 41-44, 47 and 50 are rejected under 35 U.S.C. 102(b) as being anticipated by US 2002/0022228.

US 2002/0022228 (see paragraphs 1, 32, 39, 40, 43, 55, 57, 58, 62, 79, 80, 88, 96, 104-110 and examples) teach a method for analyzing DNA repair by excision and resynthesis. The DNA containing lesion can be in a plasmid and multiples are placed on a support, including a glass slide or an array. The lesion can be chemically created or treated with UV irradiation. More than one agent can be used, for example,

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methylene in conjunction with visible light. The array is used to test multiple lesions, and the nature of an array is a solid support with divided zones for assessing different solutions. Most DNA is negatively supercoiled (as evidenced by You et al, Biophys. J.: Biophys Letters L43-L45, 2005 (previously supplied article)), therefore, absent evidence to the contrary, the plasmids used are supercoiled. There is also control (wild type) DNA. When the sample has been immobilized on the support, it is washed, and treated with DNA repair enzymes. The DNA can be labeled with fluorescence-labeled nucleotide triphosphates and scanned to detect if modifications are still present, and compared to the control. The DNA can be double-stranded. The buffer used can have a pH of 7.6. 100 pmol DNA molecules/ml are used. This reference also reads on the methods to establish a repair profile, diagnose a repair-related disease, to assess the influence of a physical or chemical treatment means on repair capacities and for screening substances capable of modulating a repair system (claims 41-44) since these methods all comprise the exact same steps.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 26-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 2002/00222288 as applied to claims 22-25, 31, 33, 38, 41-44, 47 and 50 above, and further in view of Douki et al.

US 2002/0022228 teaches all of the limitations as described above. However, it does not teach digesting the plasmids and analyzing them by HPLC coupled to mass spectrometry.

Douki et al (Nuc. Acid Res. 32(12): 3134-3142, 2003, specifically pp. 3134-44) teaches digesting DNA exposed to UV irradiation and analyzing the digested DNA by HPLC coupled with mass spectrometry. Nuclease P1 was used for the digestion.

The ordinary skilled artisan, desiring to digest DNA with P1 nuclease that has been exposed to UV irradiation and analyzing the digested DNA by HPLC coupled with mass spectrometry would have been motivated to combine the teachings of US 2002/0022228 teaching a method for analyzing DNA repair by excision and resynthesis with the teachings of Douki et al, teaching digesting DNA exposed to UV irradiation and analyzing the digested DNA by HPLC coupled with mass spectrometry, because Douki et al state that HPLC associated with tandem mass spectrometry represents an interesting alternative to achieve a more specific quantification of UV-induced DNA products. It would have been obvious to one of ordinary skill in the art because Douki et al teach that HPLC-MS can be used to quantify nucleosides that have been released by phosphodiesterases or P1 nucleases. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be

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considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over US 2002/0022228 as applied to claims 22-25, 31, 33, 38, 41-44, 47 and 50 above, and further in view of Meselson et al.

US 2002/0022228 teaches all of the limitations as described above. However, it does not teach purifying plasmids by sucrose gradient centrifugation or cesium chloride gradient centrifugation.

Meselson et al (PNAS 43(7):581-8, 1957, specifically p. 581) teaches purifying plasmids by sucrose gradient centrifugation or cesium chloride gradient centrifugation.

The ordinary skilled artisan, desiring to purify plasmids by sucrose gradient centrifugation or cesium chloride gradient centrifugation would have been motivated to combine the teachings of US 2002/0022228 teaching a method for analyzing DNA repair by excision and resynthesis with the teachings of Meselson et al, teaching purifying plasmids by sucrose gradient centrifugation or cesium chloride gradient centrifugation, because Meselson et al state that the range of the gradient can be adjusted to encompass the desired macromolecule to be purified. It would have been obvious to one of ordinary skill in the art to use sucrose gradient centrifugation or cesium chloride gradient centrifugation because Meselson et al teach that these gradients establish a gradient of macromolecules allowing for purification of the desired molecule. Given the teachings of the prior art and the level of the ordinary skilled

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artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over US 2002/0022228 as applied to claims 22-25, 31, 33, 38, 41-44, 47 and 50 above, and further in view of MPEP 2144.05.

US 2002/0022228 teaches all of the limitations as described above. However, it does not teach a plasmid concentration of 5 to 100 $\mu\text{g/ml}$.

MPEP 2144.05 teaches that optimizing concentrations is obvious.

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A. Optimization Within Prior Art Conditions or Through Routine Experimentation

Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. “[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.” *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be *prima facie* obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also *Peterson*, 315 F.3d at 1330, 65 USPQ2d at 1382 (“The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.”); *In re Hoeschele*, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see *Merck & Co. Inc. v. Biocraft Laboratories Inc.*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), *cert. denied*, 493 U.S. 975 (1989); *In re Kulling*, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997).

MPEP 2144.05

Therefore, since there is no evidence that using a concentration of 5 to 100 µg/ml of plasmid DNA is significant, it would be obvious to adjust the amount of plasmid concentration taught by US 2002/0022228 to 5 to 100 µg/ml. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

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Claims 34-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 2002/0022228 as applied to claims 22-25, 31, 33, 38, 41-44, 47 and 50 above, and further in view of Chiu et al.

US 2002/0022228 teaches all of the limitations as described above. However, it does not teach sensitizing a glass slide with an epoxy group. It does teach the support comprising different zones, as discussed above.

Chiu et al (Biochem. 374(3):625-32, 2003, specifically p. 625) teach using an epoxy group to treat a glass slide.

The ordinary skilled artisan, desiring to use an epoxy group to treat a glass slide would have been motivated to combine the teachings of US 2002/0022228 teaching a method for analyzing DNA repair by excision and resynthesis with the teachings of Chiu et al, teaching using an epoxy group to treat a glass slide, because Chiu et al state that epoxysilane will increase the binding capacity and efficiency of hybridization of DNA on the glass surface. It would have been obvious to one of ordinary skill in the art to use an epoxy group because Chiu et al teach that the enhanced binding allows the DNA to survive high-stringency washes. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 32 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 2002/0022228 as applied to claims 22-25, 31, 33, 38, 41-44, 47 and 50 above, and further in view of Zierdt et al.

US 2002/0022228 teaches all of the limitations as described above. It also teaches washing the array with PBS (phosphate buffer saline solution). However, it does not teach a buffer containing a saline solution and a nonionic surfactant.

Zierdt et al (Appl Environ Microbiol. 38(6):1166-72, 1979, specifically p. 1166) teach using a buffer containing phosphate and Tween 20.

The ordinary skilled artisan, desiring to use a buffer containing a saline solution and a nonionic surfactant would have been motivated to combine the teachings of US 2002/0022228 teaching a method for analyzing DNA repair by excision and resynthesis with the teachings of Zierdt et al, teaching a buffer containing phosphate and Tween 20, because Zierdt et al state that Tween 20 can partially block strong adherence to a filter. It would have been obvious to one of ordinary skill in the art to use a buffer containing phosphate and Tween 20 because Zierdt et al teach that it is undesirable to have molecules larger than the pore size adhering to the filter, therefore, it is beneficial to use a substance to remove some of those molecules. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

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Claims 39 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 2002/0022228 as applied to claims 22-25, 31, 33, 38, 41-44, 47 and 50 above, and further in view of Gelfand et al.

US 2002/0022228 teaches all of the limitations as described above. However, it does not teach exciting the labeled triphosphate and measuring the signal emitted.

Gelfand et al (PNAS 96: 6113-6118, 1999, specifically p. 6113-15) teach using FRET to compare a reference (control) DNA molecule to a DNA molecule which contains a lesion. The molecules are excited, and free energy is measured.

The ordinary skilled artisan, desiring to excite the labeled triphosphate and measuring the signal emitted would have been motivated to combine the teachings of US 2002/0022228 teaching a method for analyzing DNA repair by excision and resynthesis with the teachings of Gelfand et al, teaching using FRET to compare a reference (control) DNA molecule to a DNA molecule which contains a lesion, because Gelfand et al state that because of the sensitivity of fluorescence, the method requires orders of magnitude less material than other solution methods. It would have been obvious to one of ordinary skill in the art to use FRET because Gelfand et al teach that FRET has high throughput ability. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

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Claims 45 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 2002/0022228 as applied to claims 22-25, 31, 33, 38, 41-44, 47 and 50 above, and further in view of MPEP 2144.05.

US 2002/0022228 teaches all of the limitations as described above. It also teaches incubating for 1 hour and 2 hours at 37°C. However, it does not teach incubating for 3 hours, or teach incubating at 30°C.

MPEP 2144.05 teaches that optimizing concentrations is obvious.

A. Optimization Within Prior Art Conditions or Through Routine Experimentation

Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. “[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.” *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be *prima facie* obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also *Peterson*, 315 F.3d at 1330, 65 USPQ2d at 1382 (“The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.”); *In re Hoeschele*, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see *Merck & Co. Inc. v. Biocraft Laboratories Inc.*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), *cert. denied*, 493 U.S. 975 (1989); *In re Kulling*, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997).

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Therefore, since there is no evidence that incubating for 3 hours instead of two hours is critical, or that temperature of 30°C instead of 37°C is critical, it would be obvious to use 30°C or to incubate for 3 hours. Also, claim 45 reads "at a temperature of about 30°C", therefore absent evidence to the contrary, 37°C is about 30°C. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim 48 is rejected under 35 U.S.C. 103(a) as being unpatentable over US 2002/0022228 as applied to claims 22-25, 31, 33, 38, 41-44, 47 and 50 above, and further in view of Yershov et al.

US 2002/0022228 teaches all of the limitations as described above. However, it does not teach depositing the plasmids on an array with a robot.

Yershov et al (PNAS 93(10):4913-8, specifically p. 4913, 4917) teach depositing the DNA on an array with a robot.

The ordinary skilled artisan, desiring to deposit DNA on an array with a robot would have been motivated to combine the teachings of US 2002/0022228 teaching a method for analyzing DNA repair by excision and resynthesis with the teachings of Yershov et al, teaching depositing the DNA on an array with a robot, because Yershov et al state that using a robot is efficient for DNA sequence comparisons. It would have been obvious to one of ordinary skill in the art to use a robot because Yershov et al

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teach that it the robot capacity can be scaled up to allow for high concentrations of DNA to be deposited. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim 49 is rejected under 35 U.S.C. 103(a) as being unpatentable over US 2002/0022228 as applied to claims 22-25, 31, 33, 38, 41-44, 47 and 50 above, and further in view of Randerath et al.

US 2002/0022228 teaches all of the limitations as described above. However, it does not teach that the labeled triphosphate is labeled with ^{32}P .

Randerath et al (PNAS 78(10):6126-9, 1981, specifically p. 4913, 4917) teach labeling DNA with ^{32}P to test for DNA damage.

The ordinary skilled artisan, desiring to label with ^{32}P would have been motivated to combine the teachings of US 2002/0022228 teaching a method for analyzing DNA repair by excision and resynthesis with the teachings of Randerath et al, teaching labeling DNA with ^{32}P , because Randerath et al state that labeling DNA with ^{32}P provides an ultrasensitive and rapid assay. It would have been obvious to one of ordinary skill in the art to use ^{32}P because Randerath et al teach that it provides a means for detecting covalent binding of chemicals to DNA, and thus should be suitable for screening potential carcinogens. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered,

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absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Allowable Subject Matter

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHELE K. JOIKE whose telephone number is (571)272-5915. The examiner can normally be reached on M-F, 9:00-5:30.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Michele K Joike, Ph.D.
Examiner
Art Unit 1636

/David Guzo/
Primary Examiner
Art Unit 1636